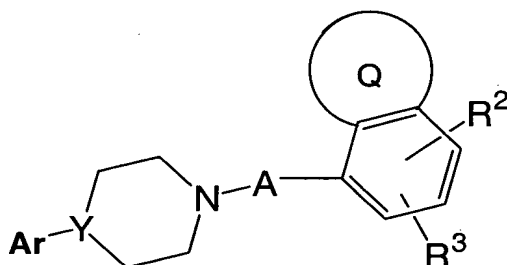


CLAIMS

1. A compound of the formula 1



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wherein Ar is 1,2-benzisothiazoyl, 1,2-benzisothiazoyl-1-oxide, 1,2-benzisothiazoyl-1-dioxide, 1,2-benzisoxazoyl, naphthyl, pyridyl, quinolyl, isoquinolyl, benzothiadiazoyl, benzotriazolyl, benzoxazolyl, benzoxazolonyl, phthalazinyl, indolyl, indanyl, 1H-indazoyl, or 3-indazoyl, and wherein Ar can optionally be substituted by one or more substituents, preferably from zero to four substituents, independently selected from halo, preferably chloro or fluoro, cyano, nitro, (C₁-C₆) alkyl optionally substituted with from one to three fluorine atoms and (C₁-C₆) alkoxy optionally substituted with from one to three fluorine atoms; with the proviso that Ar can not be attached to the piperazine ring via a phenyl ring of Ar;

Y is N or CH;

A is -(CH₂)_nCH₂-, wherein n is an integer from one to four, wherein one of the CH₂ groups that is not adjacent to the piperazine nitrogen can optionally be replaced by an oxygen atom;

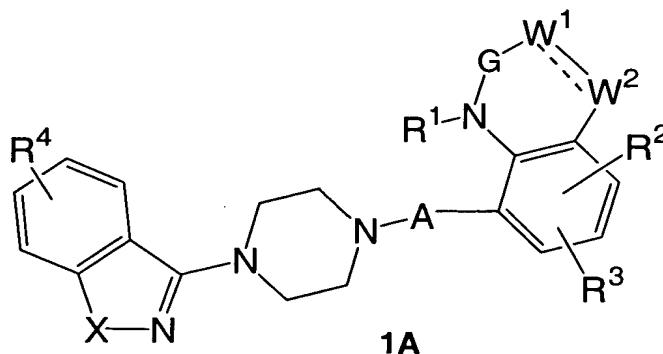
R² and R³ are independently selected from hydrogen, (C₁-C₆) alkyl optionally substituted with from one to three fluorine atoms, (C₁-C₆) alkoxy optionally substituted with from one to three fluorine atoms, halogen, nitro, cyano, amino, (C₁-C₆) alkylamino and di-(C₁-C₆) alkylamino; and

ring Q can be a saturated, unsaturated or aromatic five to seven membered monocyclic heterocyclic ring containing from one to three

heteoratoms independently selected from oxygen, nitrogen and sulfur, and wherein ring Q can be optionally substituted with from one to four substituents, preferably with two or three substituents, independently selected from amino, oxo, hydroxy, (C₁-C₆) alkyl optionally substituted with from one to three fluorine atoms, (C₁-C₆) alkoxy optionally substituted with from one to three fluorine atoms, aryl, aryl-(C₁-C₆) alkyl-, (C₁-C₆) alkenyl optionally substituted with from one to three fluorine atoms, heteroaryl and heteroaryl-(C₁-C₆) alkyl-, wherein the alkyl moieties of the aryl-(C₁-C₆) alkyl- and heteroaryl-(C₁-C₆) alkyl groups can be optionally substituted with from one to three fluoro atoms, and where the aryl and heteroaryl moieties of these groups can optionally be substituted with one or more substituents, preferably from zero to two substituents, independently selected from halo, oxo, nitro, amino, cyano, (C₁-C₆) alkyl optionally substituted with from one to three fluorine atoms and (C₁-C₆) alkoxy optionally substituted with from one to three fluorine atoms; and wherein one of the substituents on ring Q can be an alkyl chain that forms a 3 to 6 membered spirocyclic ring with a carbon atom of ring Q that is not adjacent to a heteroatom of ring Q; with the proviso that there can not be more than one oxo substituent on ring Q and there can not be more than one spirocyclic alkyl substituent on ring Q;

or a pharmaceutically acceptable salt thereof.

2. A compound of the formula



wherein X is sulfur, SO, SO₂, oxygen, or NR;

R is hydrogen, (C₁-C₆) alkyl optionally substituted with from one to three fluorine atoms, (C₁-C₆) alkoxy optionally substituted with from one to three fluorine atoms, aryl, -C(O)(C₁-C₃) alkyl, or -C(O)(C₁-C₃) alkoxy;

A is -(CH₂)_nCH₂-, wherein n is an integer from one to four, wherein one of the CH₂ groups that is not adjacent to the piperazine nitrogen can optionally be replaced by an oxygen atom;

R¹, R⁵, R⁶, R⁷, and R⁸ are independently selected from hydrogen, (C₁-C₆) alkyl optionally substituted with from one to three fluorine atoms, (C₁-C₆) alkoxy optionally substituted with from one to three fluorine atoms, aryl, aryl-(C₁-C₆) alkyl-, (C₁-C₆) alkenyl optionally substituted with from one to three fluorine atoms, heteroaryl and heteroaryl-(C₁-C₆) alkyl-, wherein the alkyl moieties of the aryl-(C₁-C₆) alkyl- and heteroaryl-(C₁-C₆) alkyl groups can be optionally substituted with from one to three fluoro atoms, and where the aryl and heteroaryl moieties of these groups can optionally be substituted with one or more substituents, preferably from zero to two substituents, independently selected from halo, nitro, amino, cyano, (C₁-C₆) alkyl optionally substituted with from one to three fluorine atoms and (C₁-C₆) alkoxy optionally substituted with from one to three fluorine atoms;

or R¹ is ZR⁹ wherein Z is -C(O)-, -C(O)O-, -C(O)NH-, -S(O)₂- or -S(O)₂NR¹⁰, wherein the hyphen to the left of each of the foregoing moieties represents the bond to NR¹ in structural formula 1A, and the hyphen to the right of each of the foregoing moieties represents the bond to R⁹ in structural formula 1A;

R², R³ and R⁴ are independently selected from hydrogen, (C₁-C₆) alkyl optionally substituted with from one to three fluorine atoms, (C₁-C₆) alkoxy optionally substituted with from one to three fluorine atoms, hydroxy, halogen, nitro, cyano, amino, (C₁-C₆) alkylamino and di-(C₁-C₆) alkylamino;

G is -C(=O)- or CH₂;

W¹ is C(R⁵)(R⁶), CHN(R⁵)(R⁶), CHC(=O)NR⁵R⁶ or C(OH)(R⁵);

W² is C(R⁷)(R⁸), CHN(R⁷)(R⁸), CHC(=O)NR⁵R⁶ or C(OH)(R⁷);

the broken line extending from W^1 to W^2 represents an optional double bond;

or one of R^5 , R^6 , R^7 , and R^8 , if present, that is attached to a carbon atom, can form, together with the carbon to which it is attached and together with another of R^5 , R^6 , R^7 , and R^8 that is present and attached to a carbon or nitrogen atom, and the carbon or nitrogen atom to which it is attached, a three to seven membered saturated or unsaturated carbocyclic or heterocyclic ring; and

with the proviso that when there is a double bond between W^1 and W^2 , then: (a) if W^1 is $C(R^5)(R^6)$, either R^5 or R^6 is absent; and (b) if W^1 is $CHN(R^5)(R^6)$, either the H atom attached to the ring carbon or R^5 or R^6 is absent; and (c) if W^1 is $C(OH)(R^5)$, either the OH group attached to the ring carbon or R^5 is absent; (d) if W^1 is $CHC(=O)NR^5R^6$, either the hydrogen attached to the ring carbon or $C(=O)NR^5R^6$ is absent; (e) if W^2 is $C(R^7)(R^8)$, either R^7 or R^8 is absent; (f) if W^2 is $CHN(R^7)(R^8)$, either the H atom or R^7 or R^8 is absent; (g) if W^2 is $C(OH)(R^7)$, either the OH group or R^7 is absent; and (h) if W^1 is $CHC(=O)NR^7R^8$, either the hydrogen attached to the ring carbon or $C(=O)NR^7R^8$ is absent;

and the pharmaceutically acceptable salts of such compounds.

3. A compound according to claim 1 that is selected from the following compounds and their pharmaceutically acceptable salts:

8-[2-(4-1,2-Benzisothiazol-3-yl-piperazin-1-yl)-ethyl]-4,4-dimethyl-3,4-dihydro-1H-quinolin-2-one;

8-[2-(4-1,2-Benzisothiazol-3-yl-piperazin-1-yl)-ethyl]-1,4,4-trimethyl-3,4-dihydro-1H-quinolin-2-one;

8-[2-(4-1,2-Benzisothiazol-3-yl-piperazin-1-yl)-ethyl]-6-fluoro-4,4-dimethyl-3,4-dihydro-1H-quinolin-2-one;

8-[2-(4-1,2-Benzisothiazol-3-yl-piperazin-1-yl)-ethyl]-3,4-dihydro-1H-quinolin-2-one hydrochloride;

8-[2-(4-1,2-Benzisothiazol-3-yl-piperazin-1-yl)-ethyl]-3,3-dimethyl-3,4-dihydro-1H-quinolin-2-one;

8-[2-(4-1,2-Benzisothiazol-3-yl-piperazin-1-yl)-ethyl]-4-phenyl-3,4-dihydro-1H-quinolin-2-one;

8-[2-(4-1,2-Benzisothiazol-3-yl-piperazin-1-yl)-ethyl]-3-methyl-1H-quinolin-2-one;

5 8-[2-(4-1,2-Benzisothiazol-3-yl-piperazin-1-yl)-ethyl]-3,4-dimethyl-1H-quinolin-2-one;

8-[2-(4-1,2-Benzisothiazol-3-yl-piperazin-1-yl)-ethyl]-4-methyl-1H-quinolin-2-one;

10 8-[2-(4-1,2-Benzisothiazol-3-yl-piperazin-1-yl)-ethyl]-4-phenyl-1H-quinolin-2-one;

8-[2-(4-1,2-Benzisothiazol-3-yl-piperazin-1-yl)-ethyl]-4-trifluoromethyl-1H-quinolin-2-one;

8-[2-(4-1,2-Benzisothiazol-3-yl-piperazin-1-yl)-ethyl]-4,4,5-methyl-3,4-dihydro-1H-quinolin-2-one;

15 8-[2-(4-1,2-Benzisothiazol-3-yl-piperazin-1-yl)-ethyl]-6-chloro-4,4-dimethyl-3,4-dihydro-1H-quinolin-2-one;

8-[3-(4-1,2-Benzisothiazol-3-yl-piperazin-1-yl)-propyl]-6-chloro-4,4-dimethyl-3,4-dihydro-1H-quinolin-2-one;

20 8-[2-(4-1,2-Benzisothiazol-3-yl-piperazin-1-yl)-ethyl]-4-isopropyl-1H-quinolin-2-one;

8-[2-(4-1,2-Benzisothiazol-3-yl-piperazin-1-yl)-ethyl]-4-ethyl-1H-quinolin-2-one;

8-[2-(4-1,2-Benzisothiazol-3-yl-piperazin-1-yl)-ethyl]-4-propyl-1H-quinolin-2-one; and

25 8-[2-(4-1,2-Benzisothiazol-3-yl-piperazin-1-yl)-ethyl]-3-ethyl-4-methyl-1H-quinolin-2-one.

4. A compound according to claim 2 wherein A is an alkylene group and n is one.

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5. A compound according to claim 2 wherein R⁴ is hydrogen and one or both of R² and R³ are hydrogen.

6. A compound according to claim 2 wherein R^1 , R^5 , R^6 , R^7 and R^8 are selected, independently, from hydrogen and (C_1-C_3) alkyl.

5 7. A compound according to claim 2, wherein one or both of R^2 and R^3 are hydrogen.

8. A pharmaceutical composition for treating a disorder or condition selected from single episodic or recurrent major depressive disorders, dysthymic disorders, depressive neurosis and neurotic depression, 10 melancholic depression including anorexia, weight loss, insomnia, early morning waking or psychomotor retardation; atypical depression (or reactive depression) including increased appetite, hypersomnia, psychomotor agitation or irritability, seasonal affective disorder and pediatric depression; bipolar disorders or manic depression, for example, 15 bipolar I disorder, bipolar II disorder and cyclothymic disorder; conduct disorder; attention deficit hyperactivity disorder (ADHD); disruptive behavior behavioral disturbances associated with mental retardation, autistic disorder, and conduct disorder; anxiety disorders such as panic disorder with or without agoraphobia, agoraphobia without history of panic 20 disorder, specific phobias, for example, specific animal phobias, social anxiety, social phobia, obsessive-compulsive disorder, stress disorders including post-traumatic stress disorder and acute stress disorder, and generalized anxiety disorders; borderline personality disorder; schizophrenia and other psychotic disorders, for example, 25 schizophreniform disorders, schizoaffective disorders, delusional disorders brief psychotic disorders, shared psychotic disorders, psychotic disorders with delusions or hallucinations, psychotic episodes of anxiety, anxiety associated with psychosis, psychotic mood disorders such as severe major depressive disorder; mood disorders associated with psychotic 30 disorders such as acute mania and depression associated with bipolar disorder; mood disorders associated with schizophrenia; delerium, dementia, and amnestic and other cognitive or neurodegenerative disorders, such as Parkinson's disease (PD), Huntington's disease (HD),

Alzheimer's disease, senile dementia, dementia of the Alzheimer's type, memory disorders, loss of executive function, vascular dementia, and other dementias, for example, due to HIV disease, head trauma, Parkinson's disease, Huntington's disease, Pick's disease, Creutzfeldt-Jakob disease, or due to multiple etiologies; movement disorders such as akinesias, dyskinesias, including familial paroxysmal dyskinesias, spasticities, Tourette's syndrome, Scott syndrome, PALSYS and akinetic-rigid syndrome; extra-pyramidal movement disorders such as medication-induced movement disorders, for example, neuroleptic-induced Parkinsonism, neuroleptic malignant syndrome, neuroleptic-induced acute dystonia, neuroleptic-induced acute akathisia, neuroleptic-induced tardive dyskinesia and medication-induced postural tremour; chemical dependencies and addictions (e.g., dependencies on, or addictions to, alcohol, heroin, cocaine, benzodiazepines, nicotine, or phenobarbitol) and behavioral addictions such as an addiction to gambling; and ocular disorders such as glaucoma and ischemic retinopathy in a mammal, including a human, comprising an amount of a compound according to claim 1, or a pharmaceutically acceptable salt thereof, that is effective in treating such disorder or condition, and a pharmaceutically acceptable carrier.

9. A method for treating a disorder or condition selected from single episodic or recurrent major depressive disorders, dysthymic disorders, depressive neurosis and neurotic depression, melancholic depression including anorexia, weight loss, insomnia, early morning waking or psychomotor retardation; atypical depression (or reactive depression) including increased appetite, hypersomnia, psychomotor agitation or irritability, seasonal affective disorder and pediatric depression; bipolar disorders or manic depression, for example, bipolar I disorder, bipolar II disorder and cyclothymic disorder; conduct disorder; attention deficit hyperactivity disorder (ADHD); disruptive behavior behavioral disturbances associated with mental retardation, autistic disorder, and conduct disorder; anxiety disorders such as panic disorder with or without agoraphobia,

agoraphobia without history of panic disorder, specific phobias, for example, specific animal phobias, social anxiety, social phobia, obsessive-compulsive disorder, stress disorders including post-traumatic stress disorder and acute stress disorder, and generalized anxiety disorders; 5
borderline personality disorder; schizophrenia and other psychotic disorders, for example, schizophreniform disorders, schizoaffective disorders, delusional disorders brief psychotic disorders, shared psychotic disorders, psychotic disorders with delusions or hallucinations, psychotic episodes of anxiety, anxiety associated with psychosis, psychotic mood 10
disorders such as severe major depressive disorder; mood disorders associated with psychotic disorders such as acute mania and depression associated with bipolar disorder; mood disorders associated with schizophrenia; delerium, dementia, and amnestic and other cognitive or neurodegenerative disorders, such as Parkinson's disease (PD), 15
Huntington's disease (HD), Alzheimer's disease, senile dementia, dementia of the Alzheimer's type, memory disorders, loss of executive function, vascular dementia, and other dementias, for example, due to HIV disease, head trauma, Parkinson's disease, Huntington's disease, Pick's disease, Creutzfeldt-Jakob disease, or due to multiple etiologies; 20
movement disorders such as akinesias, dyskinesias, including familial paroxysmal dyskinesias, spasticities, Tourette's syndrome, Scott syndrome, PALSYS and akinetic-rigid syndrome; extra-pyramidal movement disorders such as medication-induced movement disorders, for example, neuroleptic-induced Parkinsonism, neuroleptic malignant 25
syndrome, neuroleptic-induced acute dystonia, neuroleptic-induced acute akathisia, neuroleptic-induced tardive dyskinesia and medication-induced postural tremour; chemical dependencies and addictions (e.g., dependencies on, or addictions to, alcohol, heroin, cocaine, benzodiazepines, nicotine, or phenobarbitol) and behavioral addictions 30
such as an addiction to gambling; and ocular disorders such as glaucoma and ischemic retinopathy in a mammal, including a human, comprising administering to a mammal in need of such treatment an amount of a

compound according to claim 1, or a pharmaceutically acceptable salt thereof, that is effective in treating such disorder or condition.

5 10. A method according to claim 9, wherein the disorder or condition that is being treated is selected from major depression, single episode depression, recurrent depression, child abuse induced depression, postpartum depression, dysthymia, cyclothymia and bipolar disorder.

10 11. A method according to claim 9, wherein the disorder or condition that is being treated is selected from schizophrenia, schizoaffective disorder, delusional disorder, substance-induced psychotic disorder, brief psychotic disorder, shared psychotic disorder, psychotic disorder due to a general medical condition, and schizophreniform disorder.

15 12. A method according to claim 9, wherein the disorder or condition that is being treated is selected from autism, pervasive development disorder, and attention deficit hyperactivity disorder.

20 13. A method according to claim 9, wherein the disorder or condition that is being treated is selected from generalized anxiety disorder, panic disorder, obsessive-compulsive disorder, post-traumatic stress disorder, and phobias, including social phobia, agoraphobia, and specific phobias.

25 14. A method according to claim 9, wherein the disorder or condition being treated is schizophrenia with concomitant depression.

15. A method according to claim 9, wherein the disorder or condition being treated is schizophrenia with concomitant anxiety.

30 16. A method of treating a disorder or condition selected from single episodic or recurrent major depressive disorders, dysthymic disorders, depressive neurosis and neurotic depression, melancholic depression including anorexia, weight loss, insomnia, early morning waking or

psychomotor retardation; atypical depression (or reactive depression) including increased appetite, hypersomnia, psychomotor agitation or irritability, seasonal affective disorder and pediatric depression; bipolar disorders or manic depression, for example, bipolar I disorder, bipolar II disorder and cyclothymic disorder; conduct disorder; attention deficit hyperactivity disorder (ADHD); disruptive behavior disorder; behavioral disturbances associated with mental retardation, autistic disorder, and conduct disorder; anxiety disorders such as panic disorder with or without agoraphobia, agoraphobia without history of panic disorder, specific phobias, for example, specific animal phobias, social anxiety, social phobia, obsessive-compulsive disorder, stress disorders including post-traumatic stress disorder and acute stress disorder, and generalized anxiety disorders; borderline personality disorder; schizophrenia and other psychotic disorders, for example, schizophreniform disorders, schizoaffective disorders, delusional disorders, brief psychotic disorders, shared psychotic disorders, psychotic disorders with delusions or hallucinations, psychotic episodes of anxiety, anxiety associated with psychosis, psychotic mood disorders such as severe major depressive disorder; mood disorders associated with psychotic disorders such as acute mania and depression associated with bipolar disorder; mood disorders associated with schizophrenia; delirium, dementia, and amnestic and other cognitive or neurodegenerative disorders, such as Parkinson's disease (PD), Huntington's disease (HD), Alzheimer's disease, senile dementia, dementia of the Alzheimer's type, memory disorders, loss of executive function, vascular dementia, and other dementias, for example, due to HIV disease, head trauma, Parkinson's disease, Huntington's disease, Pick's disease, Creutzfeldt-Jakob disease, or due to multiple etiologies; movement disorders such as akinesias, dyskinesias, including familial paroxysmal dyskinesias, spasticities, Tourette's syndrome, Scott syndrome, PALSYS and akinetic-rigid syndrome; extra-pyramidal movement disorders such as medication-induced movement disorders, for example, neuroleptic-induced Parkinsonism, neuroleptic malignant syndrome, neuroleptic-induced acute

dystonia, neuroleptic-induced acute akathisia, neuroleptic-induced tardive dyskinesia and medication-induced postural tremour; chemical dependencies and addictions (e.g., dependencies on, or addictions to, alcohol, heroin, cocaine, benzodiazepines, nicotine, or phenobarbital) and behavioral addictions such as an addiction to gambling; and ocular disorders such as glaucoma and ischemic retinopathy in a mammal, including a human, comprising administering to said mammal:

(a) a compound of the formula 1 or a pharmaceutically acceptable salt thereof; and

(b) another pharmaceutically active compound that is an antidepressant or an anti-anxiety agent, or a pharmaceutically acceptable salt thereof;

wherein the active agents "a" and "b" are present in amounts that render the combination effective in treating such disorder or condition.

17. A pharmaceutical composition for treating a disorder or condition selected from single episodic or recurrent major depressive disorders, dysthymic disorders, depressive neurosis and neurotic depression, melancholic depression including anorexia, weight loss, insomnia, early morning waking or psychomotor retardation; atypical depression (or reactive depression) including increased appetite, hypersomnia, psychomotor agitation or irritability, seasonal affective disorder and pediatric depression; bipolar disorders or manic depression, for example, bipolar I disorder, bipolar II disorder and cyclothymic disorder; conduct disorder; attention deficit hyperactivity disorder (ADHD); disruptive behavior behavioral disturbances associated with mental retardation, autistic disorder, and conduct disorder; anxiety disorders such as panic disorder with or without agoraphobia, agoraphobia without history of panic disorder, specific phobias, for example, specific animal phobias, social anxiety, social phobia, obsessive-compulsive disorder, stress disorders including post-traumatic stress disorder and acute stress disorder, and generalized anxiety disorders; borderline personality disorder; schizophrenia and other psychotic disorders, for example,

schizophreniform disorders, schizoaffective disorders, delusional disorders
brief psychotic disorders, shared psychotic disorders, psychotic disorders
with delusions or hallucinations, psychotic episodes of anxiety, anxiety
associated with psychosis, psychotic mood disorders such as severe
5 major depressive disorder; mood disorders associated with psychotic
disorders such as acute mania and depression associated with bipolar
disorder; mood disorders associated with schizophrenia; delerium,
dementia, and amnestic and other cognitive or neurodegenerative
disorders, such as Parkinson's disease (PD), Huntington's disease (HD),
10 Alzheimer's disease, senile dementia, dementia of the Alzheimer's type,
memory disorders, loss of executive function, vascular dementia, and
other dementias, for example, due to HIV disease, head trauma,
Parkinson's disease, Huntington's disease, Pick's disease, Creutzfeldt-
Jakob disease, or due to multiple etiologies; movement disorders such as
15 akinesias, dyskinesias, including familial paroxysmal dyskinesias,
spasticities, Tourette's syndrome, Scott syndrome, PALSYS and akinetic-
rigid syndrome; extra-pyramidal movement disorders such as medication-
induced movement disorders, for example, neuroleptic-induced
Parkinsonism, neuroleptic malignant syndrome, neuroleptic-induced acute
20 dystonia, neuroleptic-induced acute akathisia, neuroleptic-induced tardive
dyskinesia and medication-induced postural tremour; chemical
dependencies and addictions (e.g., dependencies on, or addictions to,
alcohol, heroin, cocaine, benzodiazepines, nicotine, or phenobarbitol) and
behavioral addictions such as an addiction to gambling; and ocular
25 disorders such as glaucoma and ischemic retinopathy in a mammal
comprising:

(a) a compound according to claim 1 or a pharmaceutically
acceptable salt thereof;

(b) another pharmaceutically active agent that is an
30 antidepressant or an anti-anxiety agent; and

(c) a pharmaceutically acceptable carrier.

18. A method according to claim 16, wherein the disorder or condition being treated is schizophrenia.

5 19. A method according to claim 16, wherein the disorder or condition that is being treated is selected from schizophrenia, schizoaffective disorder, delusional disorder, substance-induced psychotic disorder, brief psychotic disorder, shared psychotic disorder, psychotic disorder due to a general medical condition, and schizophreniform disorder.

10 20. A method according to claim 16, wherein the disorder or condition that is being treated is selected from autism, pervasive development disorder, and attention deficit hyperactivity disorder.

15 21. A method according to claim 16, wherein the disorder or condition that is being treated is selected from generalized anxiety disorder, panic disorder, obsessive-compulsive disorder, post-traumatic stress disorder, and phobias, including social phobia, agoraphobia, and specific phobias.

20 22. A method according to claim 16, wherein the compound of formula 1 is administered to a human for the treatment of any two or more comorbid disorders or conditions selected from those disorders and conditions referred to in any of the above methods.

25 23. A method according to claim 16, wherein the disorder or condition being treated is schizophrenia with concomitant depression.

24. A method according to claim 16, wherein the disorder or condition being treated is schizophrenia with concomitant anxiety.